Amendments to the Specification

Please amend the paragraph starting on page 1, line 6, as follows:

Amphetamines have long been recognized as stimulators of CNS activity in humans. Amphetamines are believed, for example, to modulate the release and uptake of excitatory neurotransmitters, such as dopamine and norepinephrine. They are used in the treatment of attention deficit hyperactivity disorder (ADHD) in children, adolescents, adults, etc., and may also be used to treat other disorders. They can be administered alone or with other active ingredients. See, generally, WO 00/23055, USSN 60/414401 and USSN 60/431963, which are entirely incorporated by reference herein. Trade names for amphetamines include e.g., DEXEDRENE® (Dextroamphetamine Sulfate), DEXTROSTAT® (Dextroamphetamine Sulfate USP), ADDERALL® (Dextroamphetamine Saccharate, Amphetamine Aspartate, Dextroamphetamine Sulfate USP, and Amphetamine Sulfate USP) immediate-release tablets and ADDERALL XR® (Dextroamphetamine Saccharate, Amphetamine Aspartate Monohydrate, Dextroamphetamine Sulfate USP, and Amphetamine Sulfate USP) Capsules ~~Dexedrene®, DextroStat®, Adderall® immediate-release tablets and Adderall XR® Capsules~~. 57th Edition of the Physicians Desk Reference, (Thomson PDR).

Please amend the paragraph starting on page 1, line 16, as follows:

In such products, the amphetamine is typically contained in the form of one or more salts, e.g., in ~~Adderall XR® and Adderall®~~ ADDERALL XR® and ADDERALL® tablets a mixture of dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine aspartate monohydrate and amphetamine sulfate. As can be seen, the amphetamines have been used in both racemic and enantiomeric form.

Please amend the paragraph starting on page 5, line 13, as follows:

This invention includes all possible regimens of administering the two enantiomers of amphetamine, e.g., administration times during a day for either or both, relative doses, all combinations of the two enantiomers, etc, as long as the features of the invention are met. Thus, without limiting the invention in any way, modes include administering more of the d-

isomer early in the day (e.g., about 6:00 am to about 11:00 am), e.g., only d-isomer or a molar ratio of d/l of about 1.5 to about 5/1, or higher or lower, (e.g., 3/1 as in ADDERALL® ~~Adderall®~~), and then administering a higher ratio of the l-isomer later in the day (e.g., about 12:00 noon or later, e.g., 4:00 pm, 6:00 pm, etc.), e.g., only l-isomer, or a molar ratio of l/d of about 1.5 to about 5/1, or higher or lower. It is also possible to administer more l-amphetamine than d-amphetamine earlier in the day or the same amounts of each (e.g., in racemic form), as long as the increased l-ratio later in the day of this invention is achieved. Similarly, the doses of each isomer can be administered in the most varied of ways, e.g., each can be administered separately, together in a single formulation, concurrently, sequentially, etc. Thus, in a preferred embodiment, a d/l ratio greater than one can be achieved in the morning by administering, e.g., substantially only d-isomer, or e.g., a dose of ADDERALL® ~~Adderall®~~ immediate release tablets (wherein the d/l ratio is 3/1), or a dose of ADDERALL XR® ~~Adderall XR®~~ (d/l is 3/1 and a second 3/1 pulsed dose is released later in the day), or any other dose of d/l greater than one; and this can be followed by at least one more dose after the morning wherein the ratio of l/d is higher than it was in the morning dose(s) as described above, wherein such later dose is in immediate release form (e.g., over a period of about 30 – about 120 minutes) or extended, sustained or otherwise controlled release form, e.g., to achieve a first order or other release profile over a period of, e.g., about 2 to about 8 or more hours, depending on the timing of the dose, age of the patient (e.g., an adult desiring later enhanced attentiveness or a child), and other conventional considerations. Of course, the morning dose can also be formulated in various extended, sustained or otherwise controlled release forms. The released relative amounts of d- and l- amphetamine varying during or between time periods also encompass a continuous shift in d/l ratio, e.g., achieved by two different sustained release profiles provided from two different compositional portions administered at the same time (unitarily or separately) or different times; including, for example, having a continuously increasing l/d ratio from one period to the next, or within any one or two or more periods, or throughout the whole day. A constant d/l ratio may be also be present during a period or from one period to the next, as long as said periods are followed by a later period wherein the l/d ratio is increased.

Please amend the paragraph starting on page 6, line 14, as follows:

Among the many other administration regimens which are suitable for this invention are included those wherein the l-isomer is administered in a fashion such that: its plasma level is essentially constant throughout the day, e.g., in a smooth, sustained release fashion; or it achieves effective plasma levels before or after achievement of at least one effective plasma level of the d-isomer; or its plasma level is continuous or sustained throughout the day while the d-isomer is pulsed or otherwise administered in any of a wide variety of ways, including but not limited to immediate-release or the pulsing modes used in ADDERALL® ~~Adderall®~~, or USP 6,322,819, WO 00/2305, USP 6,605,300, etc.; or it is administered simultaneously with the d-isomer several times throughout a day; or in various other regimens and variations, or combinations thereof. In all instances, the molar ratio of the two isomers at any given time can remain constant or can vary in either direction consistent with the foregoing, e.g., different ratios can be administered in different pulses, and the like. Either of the isomers can be used in free base form, or preferably the l-isomer, and the other in salt form, or both can be salts or free base, or a mixture of salt and free base forms can be used, etc.

Please amend the paragraph starting on page 6, line 4 from the bottom of the page, as follows:

More of the l-isomer can be administered than currently in ADDERALL® ~~Adderall®~~ and/or in ADDERALL® ~~Adderall®~~ immediate-release tablets in a given day and/or in at least one dose; e.g., where two or three doses are pulsed or otherwise administered per day (e.g., 1-6 hours apart, preferably 2-4 hours apart, as described in, e.g., WO 00/23055), additional l-isomer can be administered separately or within one or more of the administered doses such that the total daily amount of l-isomer is increased; the amount of l-isomer in each of the usual ADDERALL XR® ~~Adderall XR®~~ or immediate-release tablet doses or pulses can be increased by including additional l-isomer in each component of the dosage form. (The weight ratio of d- to l-isomer in these ADDERALL® ~~Adderall®~~ products is precisely known from the published amounts of each amphetamine salt in ADDERALL® ~~Adderall®~~, e.g., as in the package insert for ADDERALL® ~~Adderall®~~, immediate release.)

Please amend the paragraph starting on page 32, line 16, as follows:

Catania, A. C. (1998) *Learning* (4th edition. ed.) Prentice Hall,Upper Saddle River. ~~http://vig.prenhall.com/catalog/academic/product/1,4096,0132352508,00.html~~

Please amend the paragraph starting on page 34, line 18, as follows:

A) Multi-laminated beads - Delayed-release beads containing amphetamines having l/d-isomer ratios of 1/1, 2/1, 3/1, 4/1 or containing only l-isomer are overcoated with racemic amphetamine or amphetamines that have a d/l ratio of 3/1, e.g., as in ADDERALL® ~~Adderall®~~, or with d-amphetamine alone to form a one-bead system with a total daily dose of 10, 20, 30, 40, 50 or 60 mg.

Please amend the paragraph starting on page 34, line 23, as follows:

B) Combination of delayed-release beads containing amphetamines having l/d-isomer ratios of 1/1, 2/1, 3/1, 4/1 or containing only l-isomer and instant-release powder blend containing racemic amphetamine or amphetamines that have a d/l ratio of 3/1, e.g., as in ADDERALL® ~~Adderall®~~, or d-amphetamine alone, with a total daily dose of 10, 20, 30, 40, 50 or 60 mg.

Please amend the paragraph starting on page 36, line 1, as follows:

Amphetamines having l/d-isomer ratios of 1/1, 2/1, 3/1, 4/1 or only l-isomer are compressed with pharmaceutical excipients, such as lubricants, disintegrants, glidants, bulking agents, and binding agents. Subsequently, the tablets can be coated with a polymeric layer, which provides the lag time for a pulsatile delivery. The delayed-release tablet(s) can also be encapsulated with instant-release powder blend containing racemic amphetamine or amphetamines that have a d/l ratio of 3/1, e.g., as in ADDERALL® ~~Adderall®~~, or d-amphetamine alone with a total daily dose of 10, 20, 30, 40, 50 or 60 mg, into hard gelatin capsules. The amphetamines in the instant release powder blend can also be coated over the delayed-release tablets. Additionally, it is possible to use an inlaid tablet design to

incorporate the delayed-release tablet into an instant-release matrix.

Please amend the paragraph starting on page 35, line 13, as follows:

A barrier layer can be compressed over a tablet that contains amphetamines having l/d-isomer ratios of 1/1, 2/1, 3/1, 4/1 or only l-isomer using a compression coating press. The compression coated tablets can be overcoated with racemic amphetamine or amphetamines that have a d/l ratio of 3/1, e.g., as in ADDERALL® ~~Adderall®~~, or d-amphetamine alone with a total daily dose of 10, 20, 30, 40, 50 or 60 mg, or can be encapsulated into hard gelatin capsules with an instant-release powder blend of such d-enhanced amphetamines.

Please amend the paragraph starting on page 35, line 21, as follows:

A blank layer in osmotic tablets can provide a lag time for pulsatile drug delivery. Two layered osmotic tablets, which comprise one blank layer and one layer of amphetamines having l/d-isomer ratios of 1/1, 2/1, 3/1, 4/1 or only l-isomer, are overcoated with racemic amphetamine or amphetamines that have a d/l ratio of 3/1, e.g., as in ADDERALL® ~~Adderall®~~, or d-amphetamine alone with a total daily dose of 10, 20, 30, 40, 50 or 60 mg, to form a complete system. Three layered osmotic tablets can also be formed wherein a blank layer is inserted between the two types of amphetamines layers to achieve the pulsatile drug delivery.

Please amend the paragraph starting on page 39, line 2, as follows:

Two sets are prepared. One having three compartments and the other having two compartments. Each compartment is labelled as 1st, 2nd and 3rd dose as appropriate. For the two compartment packs, designs include first dose of 10, 20, 30, 40, 50 or 60 mg of ADDERALL® ~~Adderall®~~ immediate release tablets or immediate release tablets of only d-amphetamine and for each such dose, the second compartment contains in separate embodiments, doses of total amphetamines which are the same as the first dose, but have l/d-isomer ratios of 1/1, 2/1, 3/1, 4/1 or contain only l-isomer; or contains, in separate embodiments, doses of total amphetamines which are 5%, 10%, or 20% lower than the first

dose, and have l/d isomer ratios of 1/1, 2/1, 3/1, 4/1 or contain only l-isomer. Other designs include 10, 20, 30, 40, 50 or 60 mg of ADDERALL XR® ~~Adderall XR®~~ tablets in the first pack and second doses having the l-isomer contents as descried above. In three compartment packs, in addition to the foregoing, the third dose can also have an l-isomer content as described above.